Intensive Care Med (2007) 33:1434–1443
DOI 10.1007/s00134-007-0725-9

EXPERIMENTAL

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Microdialysis of the rectus abdominis muscle for early detection of impending abdominal compartment syndrome

Received: 3 November 2006
Accepted: 7 May 2007
Published online: 19 June 2007
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Electronic supplementary material
The online version of this article (doi:10.1007/s00134-007-0725-9) contains supplementary material, which is available to authorized users.

This article is discussed in the editorial available at: http://dx.doi.org/10.1007/s00134-007-0724-x.

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Abstract *Objective:* To investigate whether microdialysis is capable of assessing metabolic derangements during intra-abdominal hypertension (IAH), and whether monitoring of the rectus abdominis muscle (RAM) by microdialysis represents a reliable approach in the early detection of organ dysfunctions in abdominal compartment syndrome (ACS). *Design:* Prospective, randomized, controlled animal study. *Setting:* University animal research facility. *Subjects:* Fifteen isoflurane-anesthetized and mechanically ventilated Sprague–Dawley rats. *Interventions:* IAH of 20 mmHg was induced for 3 h and followed by decompression and reperfusion for another 3-h period ($n = 10$). Five sham-operated animals served as controls. Microdialysis was performed in the anterior gastric wall, liver, kidney, and RAM. The anterior cervical muscles served as distant reference. Glucose, lactate, pyruvate, and glycerol was analyzed throughout the 6-h experiment. *Measurements and main results:* Prolonged IAH induced significant cardiopulmonary dysfunction and persistent abdominal organ injury. Microdialysis revealed a significant increase of lactate/pyruvate and glycerol in kidney, intestine and liver, indicating ischemia, energy failure, and cell membrane damage. In addition, at 3 h IAH glucose was significantly decreased in all organs studied. The distant reference did not show any alteration of lactate/pyruvate, glycerol, and glucose over the entire 6-h observation period. In contrast to the other organs, microdialysis of the RAM showed an early and more pronounced increase of lactate, lactate/pyruvate and glycerol already at 1 h IAH. It is noteworthy that lactate, glycerol, and glucose did not completely recover upon decompression of IAH. *Conclusions:* Our data suggest that continuous microdialysis in the RAM may represent a promising tool for early detecting IAH-induced metabolic derangements.

Keywords Microdialysis · Compartment syndromes · Rectus abdominis · Animal models · Reperfusion injuries · Abdominal injuries

Introduction

In 2004 the consensus conference of the World Society on Abdominal Compartment Syndrome (WSACS, www.wsacs.org) defined intra-abdominal hypertension (IAH) as intra-abdominal pressure (IAP) $\geq$12 mmHg [1]. The abdominal compartment syndrome (ACS) describes a condition of IAH $\geq$20 mmHg in combination with single or multiple organ dysfunction which was not previously present. Recent findings suggest that ACS is associated with an increased rate of multiple organ dysfunction syndromes (MODS) [2–5]. Furthermore, ACS has been identified to be an independent predictor for MODS and prevention of ACS has been shown to decrease the incidence of MODS [3, 5].

Prevalence of IAP $\geq$ 12 mmHg reached more than 50% and IAP $\geq$ 20 mmHg was measured in 8% of a mixed general adult ICU population during an observation period of 24 h [6]. Still, a significant percentage of intensivists are unaware of current approaches in diagnosis and management of ACS [7]. In a prospective cohort study investigating major torso trauma, ACS developed in 14% of the study population. Despite good physiological response to abdominal decompression, the rate of MODS reached 54% and mortality was 58% [8]. Early detection of impending ACS may be helpful to lower mortality. Adequate decompression with temporary abdominal closure is effective in reversing the pathophysiological effects of manifest IAH; however, this was questioned by Sugrue and coworkers who demonstrated that reduction of IAP failed to improve renal function after surgical decompression in 72% of their patients [9]. The authors concluded that earlier decompression might have been beneficial for renal function [9].

The crucial development of proinflammatory cytokine-triggered MODS in ACS may not be influenced by decompression; thus, it appears obvious that early detection and prevention of impending ACS—before the release of cytokines has occurred—is of pivotal interest in successful ACS treatment.

Microdialysis has been used in experimental and clinical settings for monitoring of energy metabolism in severe brain injury [10], liver transplantation [11], plastic surgery [12], and cardiovascular surgery [13]. An increased lactate-to-pyruvate ratio (L/P ratio) has evolved as a reliable marker for ischemia, and increased glycerol levels as an indicator for cell membrane damage [14–17].

Recent experimental studies also demonstrate that intestinal ischemia can successfully be monitored by microdialysis, placing the catheters into the peritoneal cavity [18, 19] or the lumen of the gut [20]. It is noteworthy that there is no information on whether microdialysis may be a useful tool to detect metabolic derangements of intra-abdominal organs during IAH and ACS.

In a previous study, we have demonstrated [21] that the compartment pressure of the rectus sheath (CPRS) shows good agreement with IAP in IAH up to 40 mmHg. We proposed that the rectus sheath can be considered as an intra-abdominal organ regarding IAH-induced tissue damage, because it is exposed to virtually the same pressure as the intra-abdominal structures. This finding bears potential clinical relevance, because impending ACS may be detected earlier by monitoring the metabolism of the rectus abdominis muscle (RAM) by microdialysis.

The purpose of the present study was to evaluate the potential of microdialysis to detect intra-abdominal organ damage in IAH by measuring energy metabolism in liver, kidney, and intestine. Furthermore, we analyzed the energy metabolism in the RAM to assess the value and feasibility of functional RAM monitoring for early detection of impending ACS.

Materials and methods

Animals

Fifteen Sprague–Daley rats [353 $\pm$ 29 g body weight (b. w.)] were used. The animals were kept at 22 °C on 12-h light/dark cycles with free access to tap water and standard laboratory chow. Experiments were performed in accordance with the German legislation on protection of animals and the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Anesthesia and hemodynamic monitoring

The animals were anesthetized by breathing isoflurane (Forene, Abbott, Wiesbaden, Germany). No curarization was administered. After oral intubation with a 14-G catheter (Insyte, i. v. Catheter; Vialon, Spain), the animals were mechanically ventilated with a tidal volume of 1 ml/100 g b. w. The fraction of inspired oxygen was 1.0 to provide optimal oxygenation. The positive end-expiratory pressure was set at 1 cm H_2O. A baseline respiratory rate of 60 min^{-1} was chosen to maintain normoventilation.

The animals were placed on a heating pad to maintain body temperature at 37 °C. The right jugular vein and carotid artery were cannulated for continuous monitoring of mean arterial pressure (MAP), central venous pressure (CVP), and heart rate (HR). Throughout the experiment 1 ml/100 g b. w. h^{-1} saline was substituted.

Surgical procedure

Animals were initially divided into two groups: Animals of the ACS group underwent anesthesia, intubation, cannulation, laparotomy, and 3 h of IAH (n = 10). Sham-operated controls underwent identical procedures without IAH (n = 5). After midline laparotomy, an intraperitoneal catheter (12 Ch Redon drain, Dahlhausen, Cologne, Ger-

many) was placed for fluid instillation and IAP monitoring. Microdialysis catheters (CMA/20, CMA Microdialysis AB, Stockholm, Sweden) were placed in the liver, the left kidney, and the ventral aspect of the gastric wall (see ESM S.F1). The midline laparotomy was closed with a running suture, including the peritoneal sheet, all muscle layers, and the fascia. Another microdialysis catheter was placed in the RAM before the skin was closed. A fifth microdialysis catheter was placed in the anterior cervical muscles (ACM), serving as a distant control.

IAH induction

The model of IAH used in this study has been described in detail previously [22]. All animals were allowed to stabilize for 30 min before baseline measurements of MAP, CVP, HR, BCT, and microdialysis sampling. Blood samples were collected for analysis of arterial blood gases, blood cell counts, and serum lactate.

Direct continuous measurement of IAP was performed via the intraperitoneal catheter (see ESM S.F2). The midaxillary line served as zero reference. After baseline analysis, the IAP was increased to 20 mmHg by instillation of warmed (40 °C) gelatine polysuccinate (Gelafundin 4% Infusionsloesung, Braun, Melsungen, Germany). The IAP was constantly kept at 20 mmHg for 3 h. To decompress the abdomen, the Gelafundin bag was simply put below the level of the animal and the intraperitoneal fluid was allowed to drain back into the bag by gravity. After decompression, reperfusion was monitored for an additional 3 h.

Ventilatory and circulatory adaptations were made to partially compensate for deteriorations during IAH and reperfusion. An increase in ventilation frequency ($90\,min^{-1}$) was initiated at the time of IAP increase. The respiratory rate was further increased to maximally $100\,min^{-1}$ according to arterial blood gas analysis ($pCO_2 > 60$ mmHg). During the first 60 min after decompression, a $90\,min^{-1}$ ventilation frequency allowed for correction of hypercapnia. The remaining 2 h were followed by baseline respiratory frequency ($60\,min^{-1}$). A MAP of 100 mmHg (corresponding with an abdominal perfusion pressure (APP = MAP-IAP) of 80 mmHg) was determined as fluid resuscitation endpoint to preserve adequate abdominal perfusion pressure. When MAP decreased beyond 100 mmHg, saline substitution was increased to 2 ml/100g h^{-1}, or, maximally, 4 ml/100g h^{-1}.

Blood sampling

Blood cell counts were analyzed at the beginning and end of the experiment. Analyses of arterial blood gases and serum lactate were performed every 60 min. The blood sampling before and during the experiment resulted in a total volume of 0.71 ml. At the end of the experiment, serum analyses additionally included sodium, potassium, chloride, glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, bilirubin, lactate dehydrogenase (LDH), amylase, lipase, urea, creatinine, creatine kinase (CK), and creatine kinase-MB (CK-MB) according to standard methods.

Microdialysis

The interstitial concentrations of glucose, lactate, pyruvate, and glycerol were assessed as described previously in detail [23]. The system used in our study included microprobes (CMA/20, CMA Microdialysis AB, Stockholm, Sweden) carrying a microcell that was perfused by a microinjection pump (CMA/100, CMA Microdialysis AB). The molecular cutoff of the membrane was 20,000 D. The outlet tube was connected to a fraction collector (CMA/200 F, CMA Microdialysis AB). The microcell was continuously perfused with a colloid (albumin 3%) to reduce fluid loss [24, 25]. The flow rate was 0.8 μl/min for the entire experiment, and microdialysis samples were collected in 30-min fractions for baseline measurements followed by 60-min fractions for the 6-h experimental period. The costs for the microdialysis equipment reached about 150 Euro per animal.

Statistical analysis

Data are given as mean ± SD. After proving the assumption of normality and equal variance, intergroup comparison was performed by unpaired Student's *t*-test. For inner-group comparisons, one-way ANOVA for repeated measurements and a post-hoc test including the correction of the alpha-error according to Bonferroni probabilities were performed. A p-value of < 0.05 was considered significant.

Results

IAH and reperfusion-induced systemic cardiopulmonary responses

The IAH of 20 mmHg caused a significant decrease of MAP not only during IAH, but in particular during reperfusion after decompression (Table 1). This decrease was observed despite a more vigorous fluid resuscitation compared with controls (51 ± 14 vs. 28 ± 0 ml, $p < 0.05$). The CVP progressively increased during IAH but rapidly normalized during reperfusion after decompression (Table 1). It is noteworthy that in controls hematocrit decreased from 44.0 ± 3.2 to $37.5 \pm 3.4\%$ ($p < 0.05$), whereas

Table 1 Intra-abdominal hypertension and reperfusion-induced systemic cardiopulmonary responses; *BL* baseline; *MAP* mean arterial pressure; *APP* abdominal perfusion pressure; *FS* fluid substitution; *CVP* central venous pressure; *RR* respiratory rate; *BE* base excess; *ACS* acute compartment syndrome animals ($n = 10$); *Sham* sham-operated control animals ($n = 5$)

	Baseline	1 h	2 h	3 h	4 h	5 h	6 h
MAP (mmHg)							
Sham	108 ± 16	108 ± 6	117 ± 16	111 ± 18	107 ± 14	103 ± 11	106 ± 8
ACS	116 ± 10	107 ± 13	105 ± 12	95 ± 19 [a]	93 ± 16 [a]	90 ± 14 [a]	89 ± 17 [a,b]
APP (mmHg)							
Sham	88 ± 16	88 ± 6	97 ± 16	91 ± 18	87 ± 14	83 ± 11	86 ± 8
ACS	96 ± 10	87 ± 13	85 ± 12	75 ± 19 [a]	73 ± 16 [a]	70 ± 14 [a]	69 ± 17 [a,b]
FS (ml/h)							
Sham	3.6 ± 0	3.6 ± 0	3.6 ± 0	3.6 ± 0	3.6 ± 0	3.6 ± 0	3.6 ± 0
ACS	3.6 ± 0	5.7 ± 2.8	6.0 ± 2.8	6.0 ± 2.8	6.6 ± 3.5	9.9 ± 3.0	10.2 ± 3.1
CVP (mmHg)							
Sham	3 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	3 ± 2	2 ± 1
ACS	3 ± 2	6 ± 2 [a]	7 ± 2 [a,b]	9 ± 3 [a,b]	2 ± 1 [c]	2 ± 1 [c]	2 ± 1 [c]
RR (min^{-1})							
Sham	60 ± 0	60 ± 0	60 ± 0	60 ± 0	60 ± 0	60 ± 0	60 ± 0
ACS	60 ± 0	90 ± 0	90 ± 0	93 ± 4.8	90 ± 0	60 ± 0	60 ± 0
pO_2 (mmHg)							
Sham	416 ± 61	453 ± 38	415 ± 41	392 ± 48	388 ± 50	415 ± 48	416 ± 50
ACS	396 ± 67	210 ± 76 [a,b]	131 ± 49 [a,b]	93 ± 15 [a,b]	209 ± 88 [a,b,c]	212 ± 67 [a,b,c]	200 ± 67 [a,b,c]
pCO_2 (mmHg)							
Sham	34 ± 7	35 ± 4	34 ± 7	38 ± 7	34 ± 4	36 ± 5	40 ± 5
ACS	31 ± 5	39 ± 8	49 ± 11 [a,b]	65 ± 10 [a,b]	33 ± 7 [c]	39 ± 7 [c]	40 ± 5 [c]
pH							
Sham	7.48 ± 0.03	7.42 ± 0.05	7.41 ± 0.05	7.40 ± 0.04	7.42 ± 0.02	7.43 ± 0.03	7.42 ± 0.02
ACS	7.49 ± 0.04	7.26 ± 0.05 [a,b]	7.14 ± 0.08 [a,b]	6.99 ± 0.08 [a,b]	7.22 ± 0.09 [a,b,c]	7.18 ± 0.08 [a,c]	7.17 ± 0.09 [a,b,c]
BE (mmol/l)							
Sham	0.5 ± 3.9	–2.0 ± 3.6	–3.5 ± 1.5	–2.1 ± 3.4	–2.6 ± 2.2	–1.5 ± 2.3	0.5 ± 3.0
ACS	–0.8 ± 4.9	–9.9 ± 3.2 [a,b]	–13.2 ± 2.8 [a,b]	–16.1 ± 3.0 [a,b]	–14.1 ± 4.7 [a,b]	–14.3 ± 4.1 [a,b]	–14.6 ± 3.2 [a,b]
Lactate (mmol/l)							
Sham	2.6 ± 0.2	2.3 ± 0.3	2.4 ± 0.7	2.1 ± 0.9	1.8 ± 0.9	1.6 ± 0.5 [a]	1.7 ± 0.5 [a]
ACS	2.3 ± 0.6	2.0 ± 0.6	2.3 ± 0.5	3.2 ± 0.7 [a,b]	2.6 ± 0.5 [b,c]	1.9 ± 0.4 [c]	2.6 ± 0.3 [b,c]

Data are given as mean ± SD; [a] $p < 0.05$ vs. baseline; [b] $p < 0.05$ vs. sham; [c] $p < 0.05$ vs. 3 h

Table 2 Intra-abdominal hypertension and reperfusion-induced organ injury; *ACS* abdominal compartment syndrome animals ($n = 10$); *Sham* sham-operated control animals ($n = 5$); *AST* aspartate aminotransferase; *LDH* lactate dehydrogenase

Parameter	ACS	Sham	Significance (p)
Na (mmol/l)	141.6 ± 2.3	141.7 ± 1.2	0.937
K (mmol/l)	5.0 ± 0.8	4.5 ± 0.4	0.224
Cl (mmol/l)	116.9 ± 4.6	109.2 ± 3.3	0.011
Glucose (mg/dl)	97.9 ± 31.5	153.7 ± 17.2	0.015
AST (U/l)	220.7 ± 91.3	97.0 ± 33.6	0.026
Bilirubin (mg/dl)	0.15 ± 0.08	0.09 ± 0.04	0.255
LDH (U/l)	400.7 ± 202.1	108.0 ± 58.2	0.016
Urea (mg/dl)	76.1 ± 15.7	36.9 ± 7.4	0.002
Creatinine (mg/dl)	0.39 ± 0.15	0.19 ± 0.02	0.047

Data are given as mean ± SD; Blood samples were collected after 3 h IAH and 3 h reperfusion after abdominal decompression

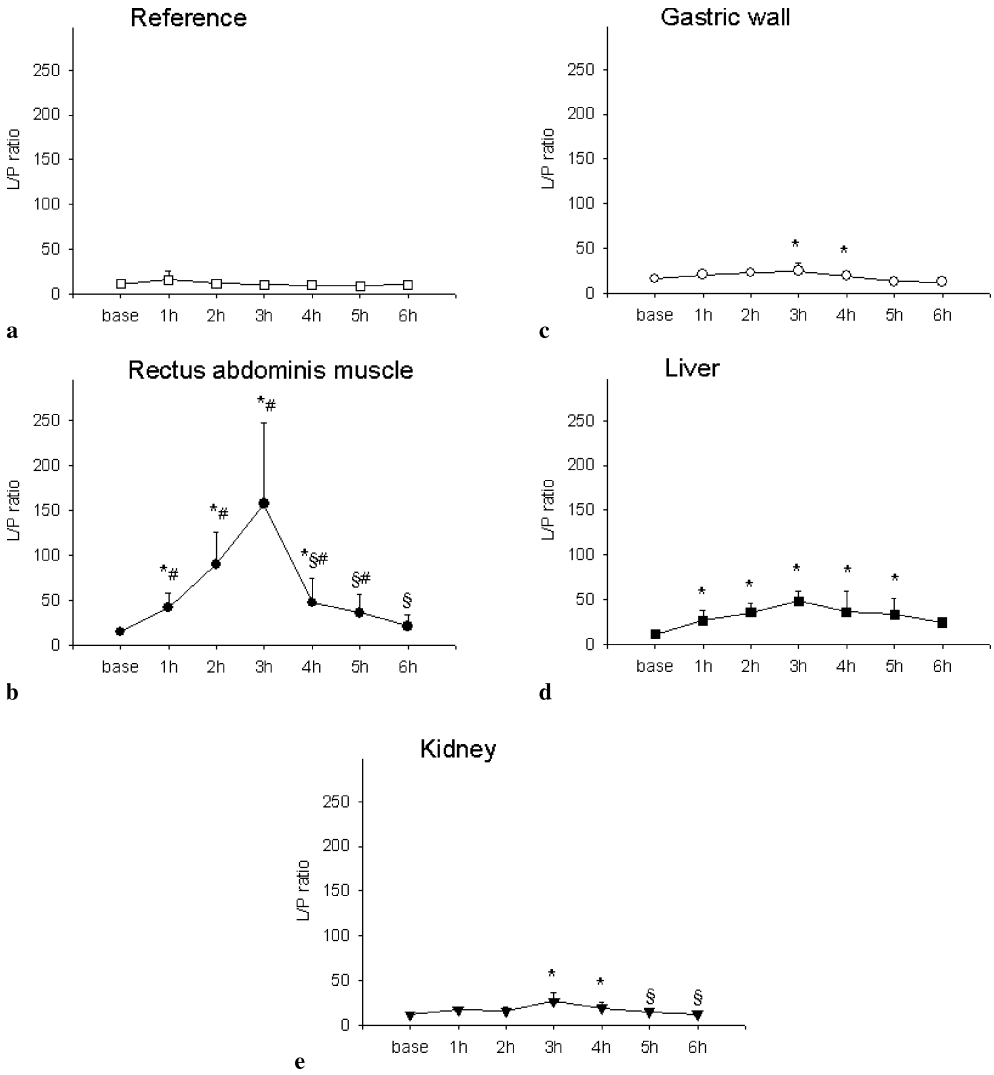

Fig. 1 The L/P ratio in the anterior cervical muscles (**a**, serving as distant reference); the rectus abdominis muscle (**b**); as well as the gastric wall (**c**); the liver (**d**); and the kidney (**e**); during baseline (*base*); 3 h of IAH (*1 h, 2 h, 3 h*), and 3 h of reperfusion after abdominal decompression (*4 h, 5 h, 6 h*); Data are given as means ± standard deviations; * $p < 0.05$ vs. baseline; § $p < 0.05$ vs. 3 h, # $p < 0.05$ vs. reference (anterior cervical muscles)

no changes were observed in ACS animals (40.5 ± 4.3 vs. 39.6 ± 6.4, $p = 0.532$). In contrast, in both groups body weight was found increased at the end of the 6-h observation period when compared with baseline (ACS: 389 ± 31 vs. 346 ± 33 g, $p < 0.05$; controls: 380 ± 15 vs. 366 ± 14 g, $p < 0.05$).

The IAH produced a combined metabolic and respiratory acidosis. A progressive hypercapnia was observed during IAH, which, however, normalized to baseline levels immediately after abdominal decompression (Table 1). In contrast, the pH and the base excess, which were found to be significantly deteriorated during IAH, did not normalize after decompression. Serum lactate levels showed a slight increase during IAH, but normal values during reperfusion (Table 1).

The PO_2 values displayed a mirror image of the pCO_2 values, indicating a generalized deterioration of gas exchange during IAH (Table 1). After decompression, pO_2 did not normalize, most probably due to manifestation of reperfusion injury with pulmonary edema in combination with emphysema and atelectasis [18].

IAH and reperfusion-induced organ injury

Analysis of serum AST as an indicator of hepatocellular injury revealed significantly ($p < 0.05$) higher values in ACS animals compared with sham controls (Table 2). The LDH showed also a fourfold increase after 3 h IAH and 3 h reperfusion. Furthermore, serum urea and creatinine showed a twofold increase in ACS animals, whereas serum glucose levels were significantly ($p < 0.05$) reduced compared with controls (Table 2). Sodium and potassium concentrations were not affected by IAH and reperfusion, but chloride showed a significant ($p < 0.05$) increase after the 6-h experimental study period (Table 2).

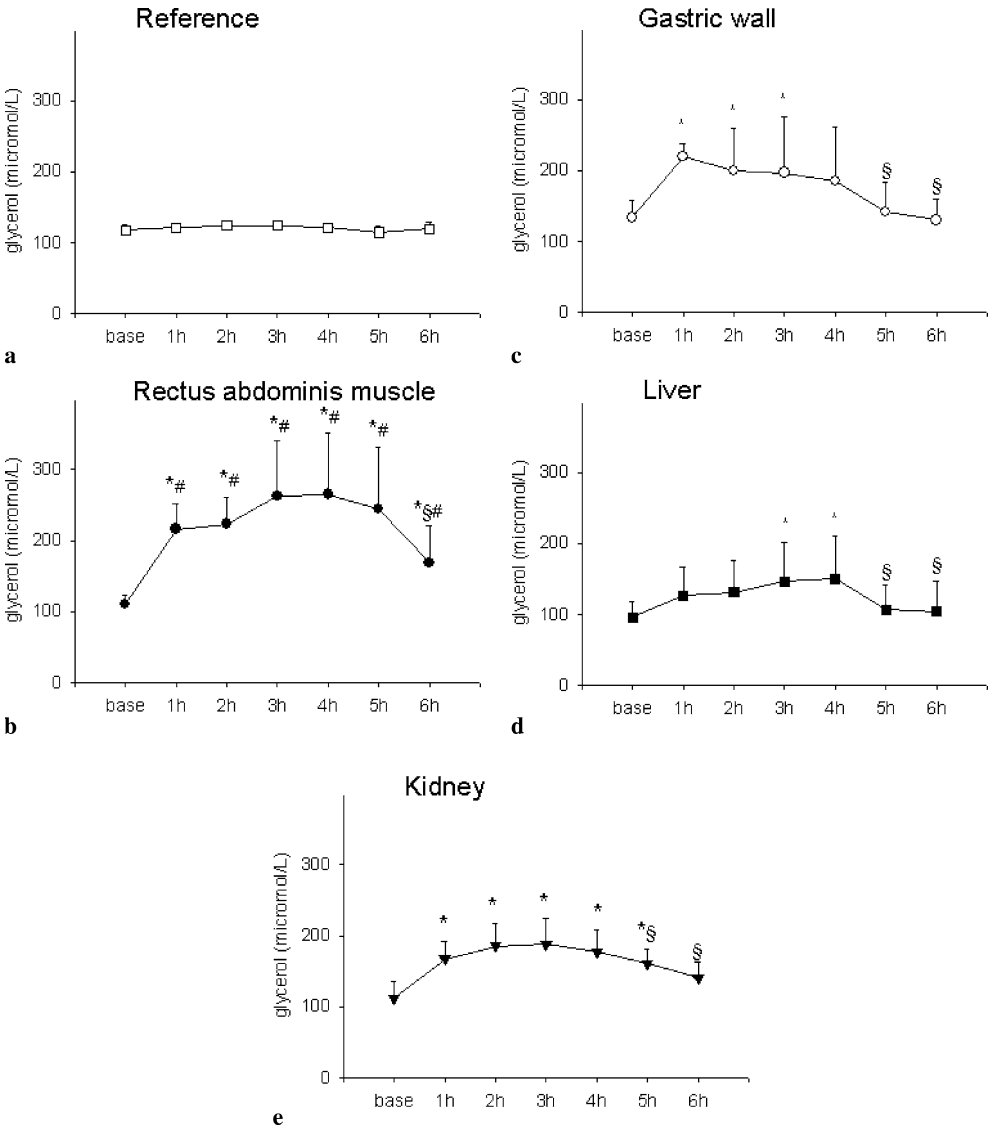

Fig. 2 Microdialysis of glycerol concentrations in the anterior cervical muscles (**a**, serving as distant reference); the rectus abdominis muscle (**b**); as well as the gastric wall (**c**); the liver (**d**); and the kidney (**e**); during baseline (*base*); 3 h of IAH (*1 h, 2 h, 3 h*) and 3 h of reperfusion after abdominal decompression (*4 h, 5 h, 6 h*); Data are given as means ± standard deviations; * $p < 0.05$ vs. baseline; § $p < 0.05$ vs. 3 h, # $p < 0.05$ vs reference (anterior cervical muscles)

IAH and reperfusion-induced alteration of tissue energy metabolism

Microdialysis analysis of the ACM demonstrated that IAH and reperfusion after decompression did not affect glucose (ESM S.F3A), lactate (ESM S.F4A), and glycerol concentration (Fig. 2a) during the entire 6-h observation period. Accordingly, the L/P ratio remained unchanged (Fig. 1a). This indicates that IAH and decompression did not affect energy metabolism in distant tissue.

In liver and gastric wall, analysis of tissue glucose concentrations revealed a progressive decrease during IAH compared with baseline (ESM S.F3C/D). Glucose concentrations in the kidney were only slightly affected (ESM S.F3E). It is noteworthy that changes of glucose concentrations in the RAM paralleled the changes observed in the liver and the gastric wall (ESM S.F3B).

Analysis of tissue lactate concentrations revealed an only slight decrease in the liver and a minor elevation in the gastric wall during IAH (ESM S.F4C/D). These changes, however, were in a range of only 25% of baseline. In kidney, no relevant changes could be observed within the entire 6-h observation period (ESM S.F4E). In contrast, in the RAM lactate concentrations increased progressively during IAH and returned toward baseline only at the end of reperfusion (ESM S.F4B).

In kidney and gastric wall tissue, but in particular in the liver, analysis of the L/P ratio showed a two- to fivefold increase during IAH, clearly distinguishing local deterioration of energy metabolism compared with the non-affected metabolism of the ACM (Fig. 1). The L/P ratio was found normalized in all tissues at the end of the 3-h reperfusion after decompression. It is noteworthy that the L/P ratio in the RAM showed a drastic increase during IAH with

values tenfold higher than baseline (Fig. 1b). After decompression the L/P ratio of the RAM declined rapidly towards values measured before IAH.

Accordingly, tissue glycerol concentrations increased significantly during IAH in liver, kidney, and gastric wall, but normalized during reperfusion after decompression (Fig. 2). In the RAM, the increase of glycerol concentrations during IAH was more pronounced compared with the other tissues, and no complete normalization was observed during reperfusion (Fig. 2b).

Because the distant reference was also taken from muscle tissue, data obtained from the RAM and the ACM may be directly compared. The L/P ratio in the RAM was significantly higher already after the first hour of IAH (42.2 vs. 11.2, $p < 0.01$). At 3 h IAH the L/P ratio was elevated 15-fold in the RAM compared with the ACM (157.6 vs. 10.6, $p < 0.05$). Accordingly, glycerol and lactate concentrations were also significantly ($p < 0.01$) increased in the RAM compared with the distant reference throughout the entire 3-h IAH period (Figs. 1, 2; ESM S.F4).

Discussion

The major findings of the present study are that (a) metabolic derangements of intra-abdominal organs during IAH of 20 mmHg can be detected by microdialysis, and (b) deteriorations of the L/P ratio and the glucose, lactate, and glycerol concentrations in the RAM indicate ACS-induced intra-abdominal organ dysfunction and injury. As the increase of ischemia markers (L/P ratio, glycerol) was early and more pronounced in the RAM compared with liver, kidney, and intestine, functional RAM monitoring by microdialysis may be a novel promising tool for early detection of impending ACS.

The deleterious effect of an increased IAP on the cardiovascular system, the lung, and various abdominal organs has been investigated in numerous experimental and clinical studies, demonstrating increased pulmonary pressure and hypoxia, decreased cardiac output and hypotension, as well as acidosis and oliguria [26–28]. Recent investigations showed a strong association between ACS and manifestation of MODS [29]. Clinical occult IAH can produce bacterial translocation and metabolically relevant ischemia of the gut and the liver [30–32]. Furthermore, the intestine has been invoked as a cytokine-generating organ after mesenteric ischemia and reperfusion. In a two-hit model of hemorrhagic shock and subsequent ACS, massive neutrophil priming provoked lung and liver injury [3]. Systemic elevation of interleukin-1 (IL-1), IL-6, IL-8, and tumor necrosis factor-α concentrations are thought to be the cause for the activation of the primed circulating neutrophils, which finally promote development of MODS [2, 4]. To avoid the onset of the "second hit" and thus development of MODS, major focus should be placed on the early recognition of a metabolically critical IAH.

Limitations of the model

The model demonstrated pathophysiological alterations consistent with IAH and ACS. During the experiment, adaptation of fluid administration and ventilation rate have been made to maintain adequate APP and tissue oxygenation. Despite marked CO_2 accumulation during IAH, the reference in the ACM demonstrated baseline conditions throughout the experiment; however, microdialysis was not performed in shams and therefore the study lacks a true control. Compared with other rodent models which maintained IAH only up to 60–90 min, metabolic changes were monitored for 3 h and 3 h of reperfusion in the herein presented model [2, 3, 22, 31].

Assessment of microcirculation in IAH

Experimental studies have demonstrated that an increase of IAP to 18–20 mmHg decreases both hepatic arterial and portal venous blood flow [32, 33]. Furthermore, an IAP of 25 mmHg results in a decrease of ileal mucosal blood flow to 63% of baseline values [31]. The analysis of blood flow may be adequate to indirectly assess metabolic alterations, as indicated by experiments demonstrating a strong correlation between superior mesenteric artery blood flow and mesenteric oxygen delivery with gastric tissue oxygenation [34]. Nonetheless, microdialysis may be superior to these indirect techniques, because more detailed information on cell energy metabolism (e. g., lactate and pyruvate), cell membrane damage (e. g., glycerol), and microvascular delivery (e. g., glucose) can be achieved. Herein, we demonstrate for the first time that the use of microdialysis is effective to indicate metabolic deteriorations during IAH of 20 mmHg. This is in line with the finding of others, demonstrating that gastric mucosal acidosis as determined by gastric tonometry can also indicate metabolic derangements during IAH [35, 36]. Although we did not perform a comparative study between microdialysis and gastric tonometry, our results indicate that the RAM is more susceptible to IAH-induced ischemia than the gastric wall; thus, microdialysis of the RAM may be preferred to gastric tonometry for early detection of critical IAH.

Alteration of tissue glucose

In the present study, we observed a decrease in tissue glucose levels during IAH. This is probably due to the locally impaired blood flow which is associated with a decreased delivery of glucose [37]. This view is supported by the results of a previous study, demonstrating with the use of an

intraperitoneally placed microdialysis catheter a decrease of glucose concentrations during local gut ischemia [18].

Alteration of tissue lactate

Lactate alone may not be a reliable marker of ischemia, because hypermetabolism also results in high lactate levels [16]. In the present study, lactate concentrations in the gastric wall, the liver, and the kidney were almost not affected by IAH and reperfusion. In contrast, the RAM showed a rapid and distinct increase of lactate during IAH. Although our study did not elucidate the cause of this differential response, it may be speculated that the local ischemia was not as severe to induce lactate accumulation in the intra-abdominal organs, but sufficient to provoke a significant increase in the RAM. This would further support the view that monitoring of metabolic changes in the RAM may be used to detect early deteriorations of an impending ACS.

Alteration of L/P ratio

The lactate-to-pyruvate (L/P) ratio is a well-known marker of cell ischemia, indicating an inadequate supply of oxygen and glucose [14, 15]. In the present study IAH provoked a significant increase of the L/P ratio in all organs studied. Nonetheless, the magnitude of the increase of the L/P ratio markedly differed between the different tissues. In the RAM, a tenfold increase was observed, whereas the increase in liver, kidney, and gastric wall was only two- to fivefold when compared with physiological baseline. This may also reflect that the metabolic deterioration during 20 mmHg IAH is more pronounced in the RAM compared with the intra-abdominal organs. The fact that the L/P ratio did not normalize immediately after decompression, in particular in muscle and liver, may indicate maintenance of ischemia due to capillary no-reflow, as described characteristically in muscle and hepatic tissue during postischemic reperfusion [38, 39]. This is in line with clinical observations which demonstrate lack of improvement of individual organ function after reduction of IAP [9].

Alteration of tissue glycerol

Microdialysis studies from the brain suggest that glycerol could act as a marker of ischemia, energy failure, and, in particular, cell membrane damage [16, 17]. The present study shows for the first time that IAH provokes a significant elevation of glycerol concentrations in liver, kidney, intestine, and muscle. It is noteworthy that the increase of glycerol concentration was markedly more pronounced in muscle than in the intra-abdominal organs and was significantly protracted in the reperfusion period. This indicates more pronounced cell damage in the muscle tissue during both IAH and reperfusion after decompression.

Relevance of RAM in IAH

Diebel and coworkers [40] demonstrated a negative correlation between increasing IAP and reduced abdominal wall blood flow in a pig model. Despite maintained cardiac output and MAP, rectus sheath blood flow, measured by Doppler laser flowmetry, decreased to 45% of baseline values when an IAP of 20 mmHg was induced; however, the critical level of perfusion was not evaluated. In a previous study we could show that the pressure measured in the rectus sheath reflects the IAP, indicating that RAM pressure measurement may serve as an alternative to intravesicular or gastric pressure measurement [21]. The results of the present study now indicate for the first time that monitoring of energy metabolism by microdialysis in the RAM may represent a valuable tool in the early detection of impending ACS by assessing IAH-induced metabolic deteriorations.

To distinguish between local and systemic responses upon induction of IAH, we additionally placed a reference probe into the distant ACM. This setting allowed not only the monitoring of systemic metabolic alterations but also made a direct comparison possible between identical tissues, e. g., the RAM directly exposed to IAH and the distant ACM not directly exposed to pressure elevation. Our data indicate that during early IAH systemic energy metabolism is not affected, whereas locally the RAM shows a marked increase of ischemia markers already within the first hour of pressure elevation. This strongly supports the view that the RAM is directly influenced by IAH, and that metabolic deteriorations can effectively be monitored by microdialysis. The fact that the metabolic alterations occur early and more pronounced in the RAM than in the liver, kidney, and gastric wall indicates an even higher susceptibility to increased IAP.

The IAH is known to decrease local blood flow in the rectus sheath [40]. In a previous study, we could demonstrate that compartment pressure in the RAM is basically similar to the IAP in the presence of IAH [21]. We are not aware whether similarly increased pressures within the intra-abdominal space and the rectus sheath lead to different alterations of microvascular blood flow with enhanced deteriorations in the rectus muscle. A more pronounced decrease of microvascular blood flow in the RAM might

be an explanation for the more pronounced increase in ischemia and cell damage markers. In fact, this explantation would further support that monitoring of the RAM by microdialysis would represent an ideal tool for early detection of IAH and ACS. This would be particularly important in case irreversible injury of the intra-abdominal organs has not already developed, as demonstrated in the present study.

Conclusion

Our study shows that deterioration of energy metabolism in IAH can successfully be monitored by microdialysis. In combination with routine IAP monitoring, continuous microdialysis of the rectus abdominis muscle may be a promising tool for detecting metabolically relevant IAH in high-risk patients before ACS is clinically apparent.

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